REMARKS

This subject application was originally filed on July 1, 2003 with 39 claims. In a restriction requirement mailed March 28, 2006, the examiner restricted the claims into 8 inventions. In response to the examiner's restriction requirement, applicants provisionally elected, with traverse, the subject matter of Group I claims (claims 1-30; expression vector or composition thereof comprising the BFA4 nucleic acid sequence), and argued that Groups I, III (claims 31-35; methods prevent/treat cancer by administering BFA4 expression vector), V (claim 36; peptides from BFA4) and VI (claim 37; method immunizing by administering peptides from BFA4) should be rejoined and examined together. Applicants also selected, with traverse, the species avipox as the expression vector to be examined, as required by the examiner.

In the latest office action, dated May 9, 2007, the examiner rejoined the claims of Groups III, IV (claims 31-35; methods prevent/treat cancer by administering BCY1 expression vector) and VI with the claims of Group I. Based on the examiner's statement on page 2 of the latest office action that, "Groups drawn to SEQ ID NO:3 will not be rejoined...", applicants believe that the examiner's rejoinder of the claims of Group IV was not intended and applicants will proceed under the assumption that the claims of Groups I, III and VI have been joined and are now to be examined together. Also in the latest office action, the examiner withdrew the species election requirement.

In response to the examiner's earlier restriction requirement, applicant's had withdrawn claims 31-39 as drawn to non-elected inventions. In light of the examiner's rejoinder of Groups III and VI claims with the claims of Group I, applicants have now indicated the status of claim 35 as "original" in the current claim listing beginning on page 2 of this response. Claims 31, 34 and 37 have been currently amended. Claims 32 and 33 have been canceled. Claims 36, 38 and 39 remain withdrawn.

Regarding the claims other than 31-39; currently amended claims are 1, 4, 9, 14, 19, 24, 26, 29, 44, 47, 52, 57 and 62; and canceled claims are 2, 3, 7, 8, 12, 13, 17, 18, 22, 23, 27, 28, 45, 46, 50, 51, 55, 56, 60 and 61. The amendments do not add new matter to the application. Therefore, the claims to be examined on the merits are 1, 4-6, 9-11, 14-16, 19-21, 24-26, 29-31, 34-35, 37, 40-44, 47-49, 52-54, 57-59 and 62-66. Based on the claims and remarks presented herein, applicants submit that the subject application is now in condition for allowance.

The Examiner's Action

In addition to rejoinder of claims and withdrawal of the species election requirement, as discussed above, the latest office action, dated May 9, 2007, sets forth the following:

-rejection of claims 21-25, 31-35 and 59-63 under 35 U.S.C. 112, second paragraph, as being indefinite;

-rejection of claims 4-35, 37, 40-43 and 47-66 under 35 U.S.C. 112, first paragraph, as failing the enablement requirement;

-rejection of claims 1-3 and 44-46 under 35 U.S.C. 102(e) as anticipated by Gish et al. (U.S. Pat. No. 6,780,586; "Gish");

-rejection of claims 1 and 44 under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as anticipated by Birse et al. (WO 02/00677; "Birse"); and

-rejection of claims 1-10 under 35 U.S.C. 102(b) as anticipated by Tartaglia et al. (Vaccine, March 2001, Vol. 19, pp. 2571-2575).

Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 21-25, 31-35 and 59-63 stand objected to under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants respectfully traverse these objections as indicated below.

Regarding the rejection of claims 21-25 and 59-63, related to co-stimulatory components, applicants direct the examiner to the application, page 2, lines 26 to 30, and specifically to the phrase "...T cell co-stimulatory molecules..." Generally, T cells are being affected by the co-stimulatory molecules/components, and numerous of these co-stimulators are recited in the specification (e.g., page 2, line 28; page 16, line 29 to page 19, line 5). Therefore, co-stimulatory components in claims 21 and 59 are not vague or indistinct. Claims 23-25 depend from claim 21 and, therefore, are also not vague or indistinct. Claim 22 has been canceled, rendering the rejection moot as to that claim.

Regarding the rejection of claims 31-35, related to SEQ ID NO.: 25 and 27, which reference peptides, applicants have amended claim 31 to recite SEQ ID NO.:1, which references a nucleic acid. Applicants direct the examiner's attention to the originally filed claim 31 which recited "SEQ ID NO.: 1 or 3" and then to applicant's subsequent responses: i) dated and received by the Patent Office on July 31, 2006, and ii) dated and received by the Patent Office on December 26, 2006. Both of those responses recite "SEQ ID NO.: 25 or 27". There was no amendment made by applicants that corresponds to this change. Therefore, applicants conclude

that they made a typographical error. To avoid any confusion, applicant's have amended claim 31 as indicated above. Claims 33 to 35 depend from claim 31. Claim 32 has been canceled. Applicants thank the examiner for detection of the error.

Rejections Under 35 U.S.C. 112, First Paragraph

Claims 4-35, 37, 40-43 and 47-66 under 35 U.S.C. 112, first paragraph, as failing the enablement requirement. Under 35 U.S.C. 112, first paragraph, the specification shall describe the invention sufficiently for one of skill to make and use it without undue experimentation. Applicants respectfully traverse these objections as indicated below.

The examiner first discusses lack of enablement with regard to the invention being "therapeutic" for cancer (pages 3-4 of office action). The facts are, with regard to peptides from BFA4, that of the 100 nonamer peptides selected for their "potential ability" to bind HLA-A*201 (Table V, pages 37-38), some of these were found to be immunoreactive for human T cells (Table VII on page 42 and discussion thereof). These T cell responses are the types of immune responses one of skill in the art would expect of peptides that induce a therapeutic effect against tumors, and these results would direct such a person to the very peptides that should be used to produce a therapeutic effect. Similarly, for a poxvirus expression vector encoding a BFA4 nucleic acid sequence, data in the specification (page 42, line 33 to page 43, line 5) show that immunization of mice with the expression vector produced T cell responses that one of skill in the art would expect for a poxvirus expression vector that would produce a therapeutic effect against tumors. As noted by the examiner on page 9 of the office action, mechanisms like deficient antigen presentation and tolerance (a mechanism by which tumor cells escape immune detection) are among those that could prevent a tumor-associated or tumor-specific antigen from inducing an immune response. The data in the specification, discussed above, indicate that these mechanisms are not preventing proteins and peptides encoded by BFA4 from producing an immune response that would be therapeutic.

Nonetheless, to align the claims more closely with the disclosure in the specification, applicants have amended claims 1, 26, 31, 37 and 44 to recite that the vectors and methods are "capable of inducing or enhancing an immune response".

The examiner next discusses lack of enablement with regard to administration of the expression vectors. Specifically, the examiner questions whether avian viral vectors could be used in practice of the invention because they are not capable of continued infection in

mammalian cells (page 5 of office action). Indeed, as discussed in Tartaglia, avipox viruses undergo an abortive infection in mammalian, including human, cells (see column 1, page 2572 of Tartaglia). The excellent safety profile of these viruses is, at least in part, due to this characteristic of these viruses. Abortive infection of human cells by these viruses, however, does not result in protein expression so low that immune responses are not generated. To the contrary, the Tartaglia paper discusses the ability of these viruses to produce their desired effects in human cells. Examples of this are found in Tartaglia in the abstract (Clinical studies...evaluating...ALVAC...have shown that this approach...can induce tumor-specific T cell responses), in column 1 of page 2572 (...recombinant ALVAC viruses were found to elicit both humoral and cellular responses against the product(s) of the inserted gene(s) in humans), in Table 2 on page 2573 (data there show that ALVAC-cytokine recombinant viruses could produce effects in cancer patients), and elsewhere. One of skill in the art would be able to practice the claimed invention using such viruses without undue experimentation.

The examiner also discusses lack of enablement with regard to administration of expression vectors to a patient (pages 5-7 of office action). The examiner cites many references, most of which point out shortcomings related to gene therapy in humans. The fact is that one must be careful in making blanket comparisons of applicant's invention, directed to inducing an immune response by administration of poxviral expression vectors, with gene therapy. While it is true that success with both techniques depends on administration to and expression in the human of recombinant vectors, there are relevant differences. For example, since the goal of gene therapy is often to complement a missing or defective genetic function, the transferred therapeutic gene normally has to be targeted to the particular defective cells, and expressed at a sustained and threshold level in order to correct the defect. This is not necessarily true when an expression vector is introduced into a human with the goal of inducing an immune response. For example, targeting the vector specifically to the tumor, for example, may not be critical. Poxviruses are capable of infecting cells of many different human tissues and, regardless of where in the body the viral infection occurs, immune responses will normally be produced and then will be effective throughout the body, including where the tumor is located. Also, sustained expression of a tumor-associated or tumor-specific antigen may not be as critical when stimulating an immune response as compared to correcting a genetic defect. Once an introduced antigen is even transiently expressed, an immune response will normally be produced and be effective. Although the level of the response may decrease over time, it can be recalled and

restimulated by various methods, including the prime-boost regimen, as disclosed in applicant's specification on page 28, lines 22-29. The fact is that sufficient data exist to enable use of poxviruses as vectors to introduce and express antigens that stimulate immune responses.

The examiner then again mentions applicant's claimed peptides and sets forth a significant list of possible problems said to support lack of enablement for the claimed peptides derived from BFA4, including the already discussed deficient antigen presentation and induction of tolerance mechanisms (pages 7-12). In response, applicants can say that, while it is usually possible to raise possibilities for why something may not work, applicants stand by the data disclosed in the application that demonstrates that at least some peptides from BFA4 are able to stimulate T cell immune responses that would enable one of skill in the art to produce an immune response in a patient that would be expected to have a therapeutic effect against tumors.

The examiner also states that claims 31-35 are not enabled for prevention of cancer (pages 12-13). As stated earlier, applicants have amended claim 31 to recite that the claimed method is "capable of inducing or enhancing an immune response" and applicants assert that the application does enable this amended claim. Claims 34 and 35 depend from claim 31. Claims 32 and 33 have been canceled.

Finally, the examiner questions whether one of skill in the art could make the NYVAC, ALVAC and TROVAC vectors recited in some of the claims. Applicants assert that sufficient information was state of the art at the time the application was filed (e.g., the patents and other references cited in the application on pages 23 and 24) to enable one of skill in the art to make these vectors without undue experimentation. As the examiner points out in the office action, applicant's specification does state that these viruses were deposited under the terms of the Budapest Treaty. Applicants remind the examiner of 37 C.F.R 1.802(c), which states that "The reference to a biological material in a specification disclosure or the actual deposit of such material by an applicant or patent owner does not create any presumption that such material is necessary to satisfy 35 U.S.C. 112 or that deposit in accordance with these regulations is or was required." Nonetheless, applicants have deposited the virus under the terms of the Budapest Treaty and are attempting to locate the additional information necessary to amend the specification in accordance with the requirements stated by the examiner on page 14 of the office action. The amendment to the specification will be made before the application is ready for issue.

Rejections Under 35 U.S.C. 102

Claims 1-3 and 44-46 stand rejected under 35 U.S.C. 102(e) as being anticipated by Gish et al. (U.S. Pat. No. 6,780,586; "Gish"). Applicants respectfully traverse these rejections.

Applicants have amended claims 1 and 44 to recite a poxvirus expression vector. Gish does not disclose a poxvirus expression vector. Therefore, Gish does not anticipate applicant's amended claims 1 or 44. Applicants have canceled claims 2, 3, 45 and 46, rendering the rejection of those claims moot. Accordingly, Applicants respectfully request withdrawal of these rejections.

Claims 1 and 44 under stand rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(c) as being anticipated by Birse et al. (WO 02/00677; "Birse"). Applicants respectfully traverse these rejections as indicated below..

Applicants have electronically searched the Sequence Listing that is part of the WO 02/00677 application and do not find applicant's SEQ ID NO:1 nor SEQ ID NO:2. The WO 02/00677 Sequence Listing contains 4300 individual sequences and, if applicants have erred in their inability to find disclosure of these sequences, applicant invites the examiner to specifically point out where applicant's SEQ ID NO:1 and/or SEQ ID NO:2 are to be found within the Sequence Listing. Lacking disclosure of these sequences, WO 02/00677 does not anticipate applicant's claims 1 or 44. Birse also does not specifically disclose poxviruses, as recited in applicant's amended claims 1 and 44. Birse also does not disclose expression vectors that are capable of inducing or enhancing an immune response, as recited in applicant's amended claims 1 and 44. Lacking such disclosures, Birse cannot anticipate applicant's claims 1 or 44. Accordingly, Applicants respectfully request withdrawal of these rejections.

Claims 1-10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Tartaglia et al. (Vaccine, March 2001, Vol. 19, pp. 2571-2575). Applicants respectfully traverse these rejections as indicated below.

Claim 1 has been amended to recite vectors comprising an immunoreactive fragment of SEQ ID NO.:1. Tartaglia does not disclose such vectors. A single nucleotide is different than an immunoreactive fragment. Therefore, Tartaglia does not anticipate applicant's amended claim 1. Claims 4, 5, 6, 9 and 10 depend either directly or indirectly from claim 1 and, therefore, are also

not anticipated by Tartaglia. Claims 2, 3, 7 and 8 have been canceled, rendering the rejections of those claims moot. Accordingly, Applicants respectfully request withdrawal of these rejections.

CONCLUSIONS

Consideration and entry of this response is respectfully requested. Applicants believe the claims are now in condition for allowance, and respectfully request that a Notice of Allowance be issued as soon as possible. The examiner is encouraged to contact the undersigned if it is believed doing so would assist in the examination of this application

Respectfully submitted,

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By: _____
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